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THE ASSAY, CHARACTERISTICS, COMPOSITION, AND ORIGIN OF OPIUM

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An Assay Procedure for Opium based on that of the Japanese Pharmacopoeia, and morphine percentages obtained on samples from various countries

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In continuation of the international programme of scientific research undertaken pursuant to resolutions 159 II C (VII) and 246 F (IX) adopted by the Economic and Social Council on 3 August 1948 and 6 July 1949 respectively, the Secretary-General is presenting the following paper by the Chief of the Narcotic Section of the National Hygienic Laboratory of Japan, as a contribution to the study of the problems of the opium assay and determination of the origin of opium.

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AN ASSAY PROCEDURE FOR OPIUM BASED ON THAT OF THE JAPANESE PHARMACOPOEIA, AND MORPHINE PERCENTAGES OBTAINED ON SAMPLES FROM VARIOUS COUNTRIES

By Haruyo Asahina

Purpose of the paper

1. The purpose of the present paper is to contribute to the study of the problems of assaying opium and determining its origin, by presenting the author's modification of the method of the Japanese Pharmacopoeia, and the results obtained on opium from various countries.

Method

2. The basic method is that of the Pharmacopoeia of Japan VI (English edition Tokyo 1952). However, there are two errors in this version, which are corrected below.

3. Another reference is the "Method of Assaying the Content of Morphine in Opium", Bulletin of the Health Organisation of the League of Nations, volume VII, extract No. 6 (1938).

4. The method of the Japanese Pharmacopoeia VI is primarily intended for standardizing powdered medicinal opium. It is a precipitation method which, like that of the United States Pharmacopoeia, does not employ any added correction. In studying it, some slight changes seemed desirable, and these are incorporated in the procedure as given below, and referred to in the notes (paragraphs 11 to 21).

Procedure for the Assay of Powdered Opium

5. Weigh accurately a quantity of 5 g. of powdered opium which has been passed through a number 5 standard mesh sieve.(1)* Transfer this accurately weighed sample into a porcelain mortar with pouring lip, add 10 cc of water and triturate the mixture well for five minutes. After the mixture has been worked into a uniform paste, add 2 g. of calcium hydroxide (fresh and more

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* Numbers in parentheses refer to the notes, paragraphs 11 to 21.

than 85 per cent purity)(2) and 40 cc. of water,(3) agitate for twenty minutes and filters.(4)

6. To about 30 cc. of the filtrate, add 0.1 g. of magnesium sulfate and digest for one minute by shaking, then add 0.3 g. of calcium hydroxide and digest for one minute in the same way. Allow this mixture to stand for one hour and then filter.

7. Measure accurately 20 cc. of the filtrate into a flask,(5) add 10 cc. of ether and 0.2 g. of ammonium chloride, and stopper the flask. Shake the mixture two or three times, diminish the pressure in the flask by removing the stopper, and then shake vigorously by hand. As soon as crystals separate from the solution, place the flask on a mechanical shaker for thirty minutes. Remove and allow to stand overnight.(6)

8. The following morning cautiously pour off the ether layer and then the aqueous layer onto a quantitative filter paper of 7 cm. diameter.(7) Rinse the crystals adhering to the inner wall of the flask with three successive 5 cc. portions of water saturated with ether. Each washing should be poured onto the filter paper so as to wash the filter paper and crystals thereon.(8) Finally wash out the mouth of the flask and upper part of the filter paper with 5 cc. of etherized water.(9)

9. Transfer the filter paper with crystals to a beaker. Completely dissolve the crystals in the flask with 15 cc. of N/10 HCl, and pour the solution into the beaker containing the filter paper. Wash the flask four times with 5 cc. portions of water,(10) and transfer all the washings to the same beaker. Titrate the excess of acid with N/10 potassium hydroxide solution. (two drops of methyl red T.S. as indicator). The end point is determined after five minutes standing.

1 cc. of N/10 HCl consumed = 28.53 mg. of $C_{17}H_{19}O_3N$(11)

10. When ferric chloride T.S. is cautiously added along the wall of the beaker the neutralized solution should produce a greenish blue colour (test for morphine).

NOTES

11. Note 1: In the League of Nations procedure, the degree of pulverization of "hard opium" is so regulated that the powder will all pass through a 0.3 mm. sieve (IV. Homogeneisation of samples).

12. Note 2: The English version of the Japanese Pharmacopoeia erroneously specifies 2 g. of potassium hydroxide instead of calcium hydroxide at this point.

13. Note 3: The total quantity of water should not exceed but be just 50 cc. during the complete procedure. A burette should be used to facilitate accurate measurements. Water and calcium hydroxide should be added gradually. Purity for the calcium hydroxide of better than 85 per cent is required by the League of Nations method. The purity should be tested as prescribed by the League method.

14. Note 4: The opinion is that it is not absolutely necessary to dry the filter paper, as prescribed by the Japanese Pharmacopoeia. It should be noted that the filter paper should not be too large for 20 cc. of filtrate.

15. Note 5: The filtrate should be clear. If turbid, results may be high; therefore if turbidity is observable in the course of the filtration the solution should be refiltered with a new filter paper. A 20 cc. volumetric pipette is used for accurate measurement of the filtrate. The use of a shaking flask as container for the 20 cc. filtrate is recommended.

16. Note 6: The stage at which the crystals separate out after the inner pressure is diminished is most important for the success of the assay. Vigorous shaking makes fine crystals separate out easily. In case of the "powdered opium", the length of time of standing prescribed by the Japanese Pharmacopoeia is twenty-four hours, for "opium alkaloids hydrochlorides", twelve to eighteen hours. However, for practical reasons, in the present modified procedure it is made just "overnight". Furthermore it is decided that "a cool place", as specified by the Pharmacopoeia, is not necessary.

17. Note 7: The filter paper is folded in four and placed in a funnel larger than the paper so as to leave about 2 mm. space above the filter paper.

18. Note 8: The phrase "the small amount of" in the Japanese Pharmacopoeia is deleted ("the small amount of crystals on the filter").

19. Note 9: The last washing with 5 cc. ether-saturated water is principally for removal of any colouring matter and acid-consuming impurities adhering to the upper part of the filter paper.

20. Note 10: This revised procedure follows that given for "opium alkaloids hydrochlorides" in the Japanese Pharmacopoeia.

21. Note 11: The procedure in the Japanese Pharmacopoeia refers to "each cc. of tenth-normal potassium hydroxide" instead of "each cc. of acid consumed" as equivalent to 28.53 mg. of morphine.

22. Analytical results

Opium samples	Loss in weight on drying (per cent)	Morphine content in per cent as determined I	as determined II	on dry basis I	on dry basis II
1. Turkey U.N. 1, Aydin D	9.36	15.62	15.55	17.23	17.16
2. Turkey U.N. 2, Afyon B	9.30	12.25	12.22	13.51	13.47
3. Turkey U.N. 3, Corum C	8.72	17.60	17.45	19.28	19.12
4. Turkey U.N. 4, Cal C	7.38	14.50	14.38	16.00	15.87
5. Turkey U.N. 5, Usak D	9.73	14.14	14.09	15.66	15.61
6. Turkey U.N. 6, Nalliban C	8.41	9.10	9.09	9.94	9.92
7. Turkey U.N. 7, Merzifon D	7.80	15.49	15.33	16.80	16.63
8. Turkey U.N. 8, Burdur B	6.77	13.70	13.70	14.69	14.69
9. Turkey U.N. 9, Kula B	7.36	13.85	13.76	14.95	14.85
10. Turkey U.N. 10, Sandikli C	7.48	11.73	11.67	12.68	12.60
11. Turkey U.N. 11, Aksehir B	7.81	12.03	12.15	13.05	13.18
12. Turkey U.N. 12, Zile D	7.84	13.75	13.76	14.92	14.93
13. Turkey U.N. 13, Isparta B	8.79	10.33	10.52	11.33	11.53

Opium samples	Loss in weight on drying (per cent)	Morphine content in per cent as determined I	as determined II	on dry basis I	on dry basis II
14. Turkey U.N. 14, Malatya D	7.80	16.41	16.17	17.80	17.54
15. Turkey U.N. 15, Export	6.83	13.62	13.60	14.62*	14.60*
16. Iran U.N. 52, Nehavand	10.19	9.34	9.38	10.40	10.44
17. Iran U.N. 49, Kerman	11.47	10.35	10.45	11.69	11.80
18. Iran U.N. 47, Fars	10.06	11.35	11.08	12.62	12.32
19. Iran U.N. 51, Khorassan	11.32	9.79	9.94	11.04	11.21
20. Iran U.N. 50, Kermanshah	10.11	10.64	10.47	11.84	11.65
21. Iran U.N. 48, Isfahan	10.51	11.25	11.00	12.57	12.29
22. India U.N. 36, Excise	11.65	9.98	9.97	11.30	11.28
23. India U.N. 34, Banaras	9.38	10.23	9.97	11.29	11.00
24. India U.N. 35, Malwa	10.53	10.69	10.63	11.95	11.88
25. Vietnam U.N. 28, Laokay, Tonkin	7.97	11.45	11.44	12.44	12.43
26. Laos U.N. 26, Luang Prabang B	9.42	6.91	6.86	7.62	7.57
27. Laos U.N. 27, Xieng Khouang B	8.78	12.15	12.38	13.32	13.57
28. Yugoslavia No.1, U.N. 24	8.93	16.26	16.30	17.85	17.90
29. Yugoslavia No. 2, U.N. 38	9.60	15.68	15.59	17.35	17.25
30. Korea No. 1, U.N. 16	10.56	2.54	2.63	2.84	2.94
31. Korea No. 2, U.N. 17	8.87	7.81	7.89	8.57	8.66
32. China, U.N. 37 B	7.60	7.73	7.85	8.37	8.50
33. Greece, U.N. 25 G	8.29	15.84	15.86	17.27	17.29
The remaining samples were opiums available in Japan					
34. Turkey	8.56	13.67	13.74	14.95	15.03
35. China (Manchuria)	8.35	11.05	10.97	12.06	11.97
36. Mongolia	9.04	10.34	10.10	11.37	11.10
37. Korea	9.60	11.16	11.06	12.35	12.23
38. China	13.12	6.20	6.19	7.13	7.12
39. Japan	9.55	10.27	10.31	11.35	11.40

* Note by the Secretariat. - The original Turkish analysis of this opium, 12.23 per cent morphine with 17.25 per cent moisture, corresponds to 14.78 per cent of morphine on the dry basis - a remarkably close check with the result now reported.

Opium samples	Loss in weight on drying (per cent)	Morphine content in per cent as determined I	as determined II	on dry basis I	on dry basis II
Samples 40 to 46 were originally dried under reduced pressure and pulverized, and the resultant opium powders were analyzed. The loss in weight by the first drying is also given, and in parentheses, the morphine content corresponding to the original condition of the raw opium					
40. Mongolia	1.92	8.37	8.42	8.53	8.58
	13.77	(7.22	7.26)		
41. Mongolia	2.82	11.91	11.97	12.26	12.32
	13.49	(10.30	10.36)		
42. Mongolia	3.49	11.91	11.94	12.34	12.37
	12.13	(10.47	10.49)		
43. China	2.61	10.41	10.12	10.69	10.39
	10.34	(9.33	9.07)		
44. China	1.06	9.16	9.09	9.26	9.19
	14.87	(7.80	7.74)		
45. China	1.74	10.14	9.92	10.32	10.10
	13.83	(8.74	8.55)		
46. China	0.65	7.52	7.28	7.57	7.33
	14.67	(6.42	6.21)		

Conclusions

23. The results obtained may be useful for comparisons with those yielded by other precipitation methods and extraction methods. In making such comparisons it should not be forgotten that the assay of the Japanese Pharmacopoeia (like that of the United States Pharmacopoeia but unlike the assays of the British Pharmacopoeia and the International Pharmacopoeia) does not add any correction.

24. The number of samples analysed is too few for hard and fast conclusions regarding the bearing of the morphine assay on origin determinations. However, it is clear that there is some relation of morphine content to origin, as shown by the tabulation in the following paragraph.

25. Classification of samples in certain groups according to morphine content on the anhydrous basis, as determined by precipitation assay.

Total number of samples and origin	Number of samples				
	Below 9 per cent	Below 11 per cent	11 to 13 per cent	Above 13 per cent	Above 14 per cent
19 - Greece, Turkey, Yugoslavia	0	1	2	16	14
13 - India, Indochina, Iran, Japan	1	2	10	1	0
14 - China, Korea, Mongolia	6	9	5	0	0

26. It may also be noted that only one sample was found from any country with less than 7 per cent of morphine on the anhydrous basis, and that the results range up to more than 19 per cent of morphine.